REMARKS

Claims 1-10, 12, 14-19, 59-66, 68, and 70-74 are presently pending. Claims 1-9 and 59-65 have been deemed allowable. Applicants gratefully acknowledge the withdrawal of all prior rejections and the allowance of claims 1-9 and 59-65.

The outstanding issues are addressed individually below.

1. The Specification

The Office Action states that the application allegedly fails to comply with the requirements set forth in 37 CFR §§ 1.821-1.825. Applicants have submitted amendments to the specification removing the executable-browser code and embedded hyperlinks. Accordingly, Applicants respectfully submit that the application, as amended, conforms to 37 CFR §§ 1.821-1.825.

2. Claim Rejections Under U.S.C. § 103

Claims 10, 12, and 14-19 were rejected as being unpatentable over Meschini *et al.* ((2000) *Int. J. Cancer* 87: 615-628) ("Meschini") in view of Fanger *et al.*, (U.S. Patent No. 5,762,930) ("Fanger") and Heidenthal *et al.* ((1999) *Biochem. Biophys. Res. Comm.* 267: 49-53) ("Heidenthal"). More specifically, the Office Action states that the term "specifically" has not been defined in the specification (see Office Action, pg. 3). Applicants respectfully traverse this rejection.

For a claimed invention to be obvious under 35 U.S.C. § 103, the references forming the basis for an obviousness rejection must teach or suggest all of the claim limitations of the claimed invention. (*In re Royka*, 490 F.2d 981 (C.C.P.A. 1974)). Moreover, it is improper to combine references where the references teach away from their combination (see MPEP § 2145 (X)(D)(2)). In addition, the words of a claim must be given their "plain meaning unless they are defined in the specification" (MPEP § 2111.01). Claim terms are presumed to take on the ordinary and customary meanings ascribed to them by those of skill in the art (see MPEP § 2111.01).

Applicants' claim 10 is directed to a method for detecting a multidrug resistant cell in a patient in which *cell-surface expressed* vimentin is detected by a vimentin binding agent that specifically binds to vimentin.

Meschini teaches the detection of *intracellular* vimentin expression (see Meschini *et al.*, p. 618). Meschini does not teach or suggest the detection of *cell-surface-expressed* vimentin.

The Fanger reference teaches generally the administration of LDL or AcLDL to patients. This reference does not teach or suggest the detection of *cell-surface-expressed* vimentin, nor that *cell-surface-expressed* vimentin is a measure of multidrug resistance of a tumor.

Heidenthal teaches that modified LDL binds to denatured vimentin *in vitro* (see Heidenthal *et al.*, p. 51). Heidenthal does not teach or suggest the detection of *cell-surface-expressed* vimentin. Heidenthal also does not teach or suggest that LDL binds to native vimentin *in vivo*.

As an initial matter, Applicants respectfully aver that the term "specifically" has a meaning that is well known to those of skill in the art. Particularly, the term "specifically" means "intended for, applying to, or acting on a particular thing" (see The American Heritage College Dictionary, 4th Ed., Houghton Mifflin Co., Boston, 2004). In the instant case, one of skill in the art would recognize that the term "specifically" is used to describe the binding of an agent to vimentin at the surface of the cell. Therefore, the term "specifically" does not require additional description in the specification.

Applicants respectfully assert that the references do not teach or suggest the detection of *cell-surface-expressed* vimentin. The primary reference cited in the Office Action, Meschini, is limited to the detection of *intracellular* vimentin, and does not teach or suggest the detection of *cell-surface-expressed* vimentin (see pg. 617-618). Meschini fails to teach or suggest that vimentin is localized to the cell surface because the reference does not show any direct or indirect evidence establishing that vimentin expression is found on the cell surface. To the contrary, the authors specifically *teach away* from the concept that vimentin is being detected at the cell surface. Meschini explicitly teaches the detection of proteins expressed only in the cell interior: vimentin, cytokeratin, actin, and tubulin, which are expressed in cytoskeletal networks (see pg. 617, Section entitled, "Cytoskeletal Organization"). Meschini describes an experiment in Figure 2 in which vimentin is shown to be associated with the cytoskeleton (see Figure 2).

This is an identical experiment to the one shown in Figure 3 in which the authors report that the staining shows "a *filament* pattern typical of adherent cells" (see Figure 3). Intermediate filaments, actin filaments, and microtubules are components of the cytoskeleton, which is an internal scaffolding located in the cytoplasm *within* the cell, not on the *cell surface* (see, *e.g.*, Alberts *et al.* Molecular Biology of The Cell. 3rd Ed., Garland Publishing, Inc. 1994, p. 787, copy enclosed). Therefore, not only does Meschini not teach or suggest the detection of *cell-surface-expressed* vimentin, but in fact, it teaches away from this concept.

In addition, Heidenthal does not teach or suggest the binding of LDL to *cell-surface-expressed* vimentin. Nor does Heidenthal teach or suggest the binding of LDL to native vimentin *in vivo*. In fact, the authors state that vimentin isolated from the cells being studied may be from *within* the cells (Heidenthal *et al.*, pg. 52). Furthermore, Heidenthal is limited to teaching that LDL binds to denatured LDL *in vitro*.

Moreover, the Fanger reference is limited to the administration of labeled LDL to patients, and does not teach or suggest the use of labeled LDL to bind to *cell-surface-expressed* vimentin, nor that *cell-surface-expressed* vimentin is a measure of multidrug resistance of a tumor.

Thus, the references cited in the Office Action, alone or in combination, do not teach or suggest the detection of *cell-surface-expressed* vimentin using a vimentin-binding agent that specifically binds to *cell surface-expressed* vimentin.

Likewise, claims 12 and 14-19, which are dependent from claim 10 and contain all of the limitations thereof, are not obviated by these references.

Accordingly, Applicants respectfully request that this § 103 rejection be reconsidered and withdrawn.

Claims 66, 68, and 70-74 were rejected as being unpatentable over Thomas *et al.* ((1999) *Clin. Can. Res.* 5: 2698-2703) ("Thomas") in view of Fanger and Heidenthal. Applicants respectfully traverse this rejection.

As stated above, for a claimed invention to be obvious in light of the prior art, the references forming the basis for an obviousness rejection must teach or suggest all of the claim limitations of the claimed invention. (*In re Royka*, 490 F.2d 981 (C.C.P.A. 1974)). Moreover, it

is improper to combine references where the references teach away from their combination (see MPEP § 2145 (X)(D)(2)).

Applicants' claim 66 is directed to a method for detecting a neoplastic cell in a patient using a vimentin-binding agent to specifically bind to *cell-surface-expressed* vimentin.

Thomas teaches detecting vimentin expression in intermediate filaments located *within* whole tissues isolated from cancer patients. Therefore, this reference does not teach or suggest the detection of *cell surface-expressed* vimentin using a vimentin-binding agent to determine whether a cell is neoplastic.

As described above, Fanger generally teaches the administration of LDL or AcLDL to patients. Fanger does not teach or suggest that vimentin expression is found at the cell surface, nor that cell-surface-expressed vimentin is indicative of a neoplastic cell or is a measure of neoplastic potential. Furthermore, this reference does not teach or suggest that the detection of *cell-surface-expressed* vimentin using vimentin-binding agents that specifically bind to *cell-surface-expressed* vimentin.

As described above, Heidenthal teaches that modified LDL binds to *cell-surface-expressed* vimentin (see Heidenthal *et al.*, pp. 51). Heidenthal does not teach or suggest that *cell-surface-expressed* vimentin is indicative of a neoplastic cell or is a measure of neoplastic potential. This reference also does not teach or suggest that the detection of *cell-surface-expressed* vimentin using vimentin-binding agents that specifically bind to *cell-surface-expressed* vimentin.

None of the references cited in the Office Action, alone or in combination, teach or suggest the detection of *cell-surface-expressed* vimentin using a vimentin-binding agent that specifically binds to *cell-surface-expressed* vimentin. Thomas teaches detection of vimentin in intermediate filaments, which exist *within* cells (see Thomas *et al.*, pg. 2700, Section entitled, "Semiquantitative Immunohistochemical Analysis of Keratin and Vimentin in IFs in Breast Tumor Cells" and pg. 2701, Section entitled, "Demonstration of Keratin and Vimentin in a FNAB"). Thomas explicitly teaches that the vimentin staining pattern in Figure 1 is showing "keratin [intermediate filaments] and vimentin [intermediate filaments]" (see Figure 1). Thomas *et al.* further teaches that the staining shown in Figure 3 is directed to intermediate filament staining to determine whether the existence of vimentin intermediate filaments is indicative of

poor prognosis (see pg. 2701, Section entitled, "Demonstration of Keratin and Vimentin in a FNAB"). It is well known in the art that intermediate filaments are located *within* cells to provide support and organelle positioning (see, *e.g.*, Alberts *et al.* Molecular Biology of The Cell. 3rd Ed., Garland Publishing, Inc. 1994, p. 788). Therefore, this reference does not teach or suggest, but teaches away from, the conclusion that vimentin is expressed on the cell surface.

Similarly, Heidenthal does not teach or suggest the detection *cell-surface-expressed* vimentin. As described above, this reference is limited to teaching that LDL binds to denatured LDL *in vitro*.

Additionally, Fanger does not teach or suggest the use of labeled LDL to bind to *cell-surface-expressed* vimentin, nor that *cell-surface-expressed* vimentin is a measure of multidrug resistance of a tumor.

The combination of these references does not result in Applicants' claim 66. Likewise, claims 68 and 70-74, which are dependent on claim 66, and thus contain all the limitations thereof, are also not obviated by the combination of these references.

Accordingly, Applicants respectfully request that this § 103 rejection be reconsidered and withdrawn.

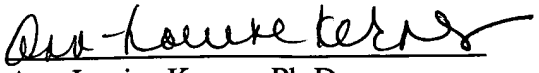
CONCLUSIONS

In view of the arguments set forth above, Applicants respectfully submit that the outstanding rejections contained in the Office Action mailed on May 3, 2006 should be reconsidered and withdrawn.

No fees are due in connection with this response. However, please charge any underpayments or credit any overpayments to Deposit Account No. 08-0219.

If the Examiner believes that any further discussion of this communication would be helpful, please contact the undersigned at the telephone number provided below.

Respectfully submitted,



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August 3, 2006
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